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EXAMINER

MUMMERT, STEPHANIE KANE

ART UNIT	PAPER NUMBER
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1637

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/852,968	Applicant(s) CHAN, EUGENE Y.	
	Examiner STEPHANIE K. MUMMERT	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 September 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 178-181 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 178-181 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's amendment filed on September 21, 2009 is acknowledged and has been entered. Claims 178 and 179 are amended. Claims 1-177 have been canceled. Claims 178-181 have been added. Claims 178-181 are pending.

Claims 178-181 are discussed in this Office action.

Response to Arguments

Applicant's arguments, see p. 6, filed September 21, 2009, with respect to the rejection(s) of claim(s) 179 and 181 under 35 U.S.C. 102 and 103 as being anticipated or obvious over Rigler have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Heid.

All of the remaining amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This action is made NON-FINAL to address new grounds of rejection.

Previous Grounds of Rejection

The rejection of claims as lacking enablement is withdrawn in view of Applicant's amendment and argument regarding the interpretation of the claim.

The rejection of claim 179 as being anticipated by Rigler is withdrawn.

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/037921 filed February 12, 1997, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The newly added claims specifically recite "emits the fluorescence signal in the absence of fluorescence resonance energy transfer". However, the prior filed application is directed entirely to detection using RET or FRET detection. A careful review of the disclosure did not indicate the embodiment(s) claimed herein, where the marker is exposed to electromagnetic radiation and the signal is detected. Therefore, the claims will be afforded the filing date of the priority document with proper support for the claims, 60/064687, filed November 5, 1997.

Terminal Disclaimer

The terminal disclaimer filed on September 21, 2009 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of 6,355,420 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 178 is rejected under 35 U.S.C. 102(b) as being anticipated by Rigler et al. (Journal of Biotechnology, 1995, vol. 41, p. 177-186). Rigler teaches single molecule detection using fluorescence spectroscopy (Abstract).

With regard to claim 178, Rigler teaches a method for analyzing a nucleic acid comprising providing a nucleic acid, labeled with a unit specific marker, detecting a fluorescent signal from the unit specific marker bound to the nucleic acid after exposure to electromagnetic radiation, storing a signature of signals to analyze the nucleic acid, wherein the nucleic acid is moved relative to the electromagnetic radiation by a polymerase (p. 182, col. 2 to p. 183, col. 1, see also, legend Figure 7, where M13-DNA molecule is labeled with rhodamine dUTP using an 18-mer primer using Klenow polymerase and where the where the nucleic acid moves during labeling with the polymerase), and the unit specific marker is labeled with a fluorophore that emits the fluorescent signal in the absence of fluorescence resonance energy transfer (Figure 7

legend, where rhodamine emits a fluorescent signal, as detected in the figure; p. 183, col. 1, where the phage DNA is shown in the form of 'specific' photon bursts).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 180 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rigler as applied to claims 178, and further in view of Vurek et al. (US Patent 5,119,463; June 1992). Rigler teaches single molecule detection using fluorescence spectroscopy (Abstract).

Regarding claims 180, while Rigler teaches an apparatus comprising a laser for detection, Rigler is not specific regarding the presence of a waveguide. Vurek teaches the use of a waveguide in the detection (Abstract).

With regard to claim 180, Vurek teaches an embodiment of claim 178, wherein the electromagnetic radiation is transported through a waveguide (Abstract, Figure 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have incorporated a waveguide of the type described by Vurek into the method of fluorescence detection of Rigler to arrive at the claimed invention with a reasonable expectation for success. As taught by Vurek, "The optical waveguide carries light signals at different wavelengths for monitoring oxygen concentration, carbon dioxide concentration, and

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pH levels. The probe is designed so that light signals used to monitor carbon dioxide concentration are optically prevented from impinging on the sensor used to monitor (Abstract)". Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have incorporated a waveguide of the type described by Vurek into the method of fluorescence detection of Rigler to arrive at the claimed invention with a reasonable expectation for success.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 178 and 180 recites the limitation "by a polymerase" in the final step of the claim.

There is insufficient antecedent basis for this limitation in the claim.

The method recites a nucleic acid, labeled with a unit specific marker and the detection of a signal. There is no mention or requirement in the claim for labeling with a polymerase.

Claims 178-181 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "wherein the nucleic acid is moved relative to the electromagnetic radiation" in claim 178 and the term "moving a nucleic acid past electromagnetic radiation using a polymerase" in claim 179 is vague and indefinite. The recitation that the nucleic acid is moved relative to the radiation could imply that the polymerase is held stationary and the nucleic acid is

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moved. However, the claim does not recite or require that the polymerase is tethered to the apparatus, or held in place in some way. Clarification is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 178-179 are rejected under 35 U.S.C. 102(b) as being anticipated by Higuchi et al. (Nature Biotechnology, 1993, vol. 11, p. 1026-1030). Higuchi teaches single molecule detection using fluorescence spectroscopy (Abstract).

With regard to claim 178, Higuchi teaches a method for analyzing a nucleic acid comprising providing a nucleic acid, labeled with a unit specific marker, detecting a fluorescent signal from the unit specific marker bound to the nucleic acid after exposure to electromagnetic radiation, storing a signature of signals to analyze the nucleic acid, wherein the nucleic acid is moved relative to the electromagnetic radiation by a polymerase (p. 1030, col. 1, materials and methods, where PCR with a polymerase is practiced, where annealing and extension steps are monitored through EtBr fluorescent label, a “unit specific marker”; Figure 2, Figure 3B, p. 1026, where the signal is detected and stored for each cycle of amplification and therefore the polymerase is moved relative to the radiation; p. 1030, col. 2, where the radiation is provided as UV irradiation).

With regard to claim 179, Higuchi teaches a method for identifying a unit specific marker bound to a nucleic acid comprising moving a nucleic acid past electromagnetic radiation using a

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polymerase, exposing a labeled unit specific marker bound to the nucleic acid to the electromagnetic radiation (p. 1030, col. 1, materials and methods, where PCR with a polymerase is practiced, where annealing and extension steps are monitored through EtBr fluorescent label, a “unit specific marker”; Figure 2, Figure 3B, p. 1026, where the signal is detected and stored for each cycle of amplification and therefore the polymerase is moved relative to the radiation; p. 1030, col. 2, where the radiation is provided as UV irradiation), and detecting an electromagnetic radiation signal from the labeled unit specific marker in the absence of fluorescence resonance energy transfer (p. 1030, col. 2, where the radiation is provided as UV irradiation; p. 1030, col. 1, materials and methods, where PCR with a polymerase is practiced, where annealing and extension steps are monitored through EtBr fluorescent label, a “unit specific marker”, in the absence of FRET; see Figure 2, Figure 3B).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 180-181 are rejected under 35 U.S.C. 103(a) as being unpatentable over Higuchi as applied to claims 178-179, and further in view of Vurek et al. (US Patent 5,119,463; June 1992). Rigler teaches single molecule detection using fluorescence spectroscopy (Abstract).

Regarding claims 180, while Higuchi teaches an apparatus comprising a radiation source for detection, Higuchi is not specific regarding the presence of a waveguide. Vurek teaches the use of a waveguide in the detection (Abstract).

With regard to claim 180, Vurek teaches an embodiment of claim 178, wherein the electromagnetic radiation is transported through a waveguide (Abstract, Figure 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have incorporated a waveguide of the type described by Vurek into the method of fluorescence detection of Higuchi to arrive at the claimed invention with a reasonable expectation for success. As taught by Vurek, “The optical waveguide carries light signals at different wavelengths for monitoring oxygen concentration, carbon dioxide concentration, and pH levels. The probe is designed so that light signals used to monitor carbon dioxide concentration are optically prevented from impinging on the sensor used to monitor (Abstract)”. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have incorporated a waveguide of the type described by Vurek into the method of fluorescence detection of Higuchi to arrive at the claimed invention with a reasonable expectation for success.

Response to Arguments

Applicant's arguments filed September 21, 2009 have been fully considered but they are not persuasive. Applicant's arguments with respect to claims 178-179 have been considered but are moot in view of the new ground(s) of rejection. However, insofar as Applicant's arguments apply to claim 178 against Rigler, Applicant's arguments will be briefly addressed.

Applicant traverses the rejection of claims 178-179 as being anticipated by Rigler. Applicant asserts "Rigler does not teach a method for detecting signals from a unit specific marker bound to a nucleic acid that is moved relative to electromagnetic radiation by a polymerase" (p. 5 of remarks). Applicant argues that "the plot provided in Figure 7 shows the autocorrelation function of single M13-DNA molecules, that have been labeled by incorporation of rhodamine dUTP" and that Rigler "does not teach that the nucleic acids are attached to the polymerase during signal detection, and nor does it teach that the nucleic acids are moved relative to the electromagnetic radiation" (p. 6 of remarks).

These arguments have been considered, but are not persuasive for a variety of reasons. First of all, and most importantly, while Applicant more clearly states the components and steps of the invention in claim 179, claim 178 does not require that a polymerase is used for labeling, only that the nucleic acid is labeled with a unit specific marker with a non-FRET label. Therefore, as noted in the 112 rejection stated above, the claims are lacking antecedent basis for the wherein clause which requires that the nucleic acid is moved relative to the electromagnetic radiation. Further, the consideration of this feature also raises a 112, 2nd issue because it appears to imply that the polymerase is held stationary and the nucleic acid is moved along by the polymerase, while the claim does not require or recite that the polymerase is tethered. Therefore, in the absence of limitations which specifically require that the polymerase must be tethered during extension, the claims will be interpreted broadly as reading either on any incorporation of fluorescent labels by a polymerase. In the case of claim 178, the claim will be interpreted as reading on detection of fluorescent labels in the presence of a polymerase, even if the incorporation or labeling is not actively occurring. Rigler teaches the elements of the method,

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fluorescent labeling with a non-FRET label and detection of a signal emitted after exposure to electromagnetic radiation. Therefore, the rejection over Rigler is maintained and the new rejections noted above are explained.

Pertinent Prior Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Nie et al. (1995, Anal. Chem., 67(17), p. 2849-2857) teaches real time detection of single molecules using confocal fluorescence microscopy (Abstract).

Conclusion

All claims stand rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEPHANIE K. MUMMERT whose telephone number is (571)272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Stephanie K. Mummert/
Patent Examiner, Art Unit 1637

SKM